

U.S.S.N. 09/978,333

Filed: October 15, 2001

AMENDMENT AND RESPONSE TO OFFICE ACTION

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Amendment

In the Claims

1-6. (canceled)

7. (twice amended) A method for targeted recombination of a nucleic acid molecule comprising the steps of:

a) providing a ~~single-stranded~~ single-stranded oligonucleotide having a sequence that forms a ~~triple-stranded~~ triple-stranded nucleic acid molecule ~~that hybridizes by hybridizing~~ with a target sequence ~~double-stranded~~ in a double-stranded nucleic acid molecule ~~and with a Kd~~ of less than or equal to 2×10^{-6} 10^{-7} ; and

b) providing a donor nucleic acid such that recombination of the donor nucleic acid which recombines into the target sequence, is induced by triple helix formation between the ~~single-stranded~~ single-stranded oligonucleotide and ~~double-stranded~~ the double-stranded nucleic acid molecule.

8. (currently amended) The method of claim 7, wherein the ~~single-stranded~~ single-stranded oligonucleotide is between 10 and 60 nucleotides in length.

9. (currently amended) The method of claim 7, wherein the ~~single-stranded~~ single-stranded oligonucleotide is tethered to the donor ~~DNA fragment~~ nucleic acid.

10. (currently amended) The method of claim 7 wherein the ~~double-stranded~~ double-stranded nucleic acid molecule encodes a protein and the targeted recombination of the donor nucleic acid with the double-stranded nucleic acid molecule alters the activity of the protein encoded by the double-stranded nucleic acid molecule.

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11. (original) The method of claim 7, wherein the double-stranded nucleic acid molecule is selected from the group consisting of a gene, an oncogene, a defective gene, a viral genome, and a portion of a viral genome.

12. (currently amended) The method of claim 7, wherein the donor ~~fragment~~ nucleic acid is at least 30 nucleotide residues in length.

13-14. (canceled)

15. (twice amended) The method of claim 7 to produce heritable changes in the genome of an intact human or animal further comprising the steps of:

~~injecting an~~ administering the single-stranded oligonucleotide into an intact human or animal having a sequence that forms a triple-stranded nucleic acid molecule with a the target region sequence of located in the genome of the intact human or animal, and having a Kd of less than 2×10^{-6} , wherein the the oligonucleotide binds to the the target region sequence with a Kd of less than or equal to 2×10^{-7} , and mutates the the target region sequence.

16. (original) The method of claim 15 wherein the oligonucleotide is between 10 and 60 nucleotides in length.

17. (original) The method of claim 15 wherein the oligonucleotide is dissolved in a physiologically acceptable carrier.

18. (original) The method of claim 15 wherein the oligonucleotide is recombinagenic.

19. (currently amended) The method of claim 18 wherein the oligonucleotide stimulates recombination of an exogenously supplied ~~DNA-fragment~~ donor nucleic acid with the target region sequence of the genome.

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20. (currently amended) The method of claim 18 wherein the oligonucleotide stimulates recombination of a ~~tethered DNA fragment~~ donor nucleic acid that is tethered to the oligonucleotide with the target ~~region~~ sequence of the genome.

21. (currently amended) The method of claim 15 wherein the target ~~region~~ sequence is selected from the group consisting of a gene, an oncogene, a defective gene, a viral genome, and a portion of a viral genome.

22. (currently amended) The method of claim 21 wherein the gene is a defective - hemoglobin gene, cystic fibrosis gene, ~~xeroderma~~ xeroderma pigmentosum gene, nucleotide excision repair pathway gene, or hemophilia gene.

23. (original) The method of claim 15 wherein the oligonucleotide is composed of homopurine or homopyrimidine nucleotides.

24. (previously presented) The method of claim 15 wherein the oligonucleotide is composed of polypurine or polypyrimidine nucleotides.

25. (currently amended) The method of claim 9 wherein the donor ~~fragment~~ nucleic acid is between 10 and 40 nucleotides.